CLAIMS

We claim:

1. A method executed by a computer under the control of a program, said computer including a memory for storing said program, said method comprising the steps of:

(A) receiving a protein backbone structure with variable residue positions;

(B) establishing a group of potential rotamers for each of said variable residue positions, wherein at least one variable residue position has rotamers from at least two different amino acid side chains; and

(C) analyzing the interaction of each of said rotamers with all or part of the remainder of said protein backbone structure to generate a set of optimized protein sequences, wherein said analyzing step includes a Dead-End Elimination (DEE) computation.

2. A method executed by a computer under the control of a program, said computer including a memory for storing said program, said method comprising the steps of:

(A) receiving a protein backbone structure with variable residue positions;

(B) classifying each variable residue position as either a core, surface or boundary residue;

(C) establishing a group of potential rotamers for each of said variable residue positions, wherein at least one variable residue position has rotamers from at least two different amino acid side chains; and

(D) analyzing the interaction of each of said rotamers with all or part of the remainder of said protein to generate a set of optimized protein sequences.

3. A method according to claim 2 wherein said analyzing step comprises a DEE computation.

4. A method according to claim 1 or 2 wherein said set of optimized protein sequences comprises the globally optimal protein sequence.

5. A method according to claim 1 or 3 wherein said DEE computation is selected from the group consisting of original DEE and Goldstein DEE.

6. A method according to claim 1 or 2 wherein said analyzing step includes the use of at least one scoring function.

7. A method according to claim 6 wherein said scoring function is selected from the group consisting of a Van der Waals potential scoring function, a hydrogen bond potential scoring function, an atomic solvation scoring function, an electrostatic scoring function and a secondary structure propensity scoring function.

8. A method according to claim 6 wherein said analyzing step includes the use of at least two scoring functions.

9. A method according to claim 6 wherein said analyzing step includes the use of at least three scoring functions.

10. A method according to claim 6 wherein said analyzing step includes the use of at least four scoring functions.

11. A method according to claim 1 or 2 further comprising testing at least one member of said set to produce experimental results.

12. A method according to claim 4 further comprising

(D) generating a rank ordered list of additional optimal sequences from said globally optimal protein sequence.

13. A method according to claim 12 wherein said generating includes the use of a Monte Carlo search.

14. A method according to claim 2 wherein said analyzing step step comprises a Monte Carlo computation.

15. A method according to claim 12 further comprising:

(E) testing some or all of said protein sequences from said ordered list to produce potential energy test results.

16. A method according to claim 15 further comprising:

(F) analyzing the correspondence between said potential energy test results and theoretical potential energy data.

17. An optimized protein sequence generated by the method of claim 1 or 2.

18. A nucleic acid sequence encoding a protein sequence according to claim 17.

19. An expression vector comprising the nucleic acid of claim 18.

20. A host cell comprising the nucleic acid of claim 18.

21. A protein having a sequence that is at least about 5% different from a known protein sequence and is at least 20% more stable than the known protein sequence.

22. A computer readable memory to direct a computer to function in a specified manner, comprising:

a side chain module to correlate a group of potential rotamers for residue positions of a protein backbone model;

a ranking module to analyze the interaction of each of said rotamers with all or part of the remainder of said protein to generate a set of optimized protein sequences.

23. A computer readable memory according to claim 22 wherein said ranking module includes a van der Waals scoring function component.

24. A computer readable memory according to claim 22 wherein said ranking module includes an atomic solvation scoring function component.

25. A computer readable memory according to claim 22 wherein said ranking module includes a hydrogen bond scoring function component.

26. A computer readable memory according to claim 22 wherein said ranking module includes a secondary structure scoring function component.

27. A computer readable memory according to claim 22 further comprising

an assessment module to assess the correspondence between potential energy test results and theoretical potential energy data.